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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,845	07/23/2001	Shozo Shoji	MIT-C102	1190

30132 7590 07/01/2003

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EXAMINER
PARKIN, JEFFREY S

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/889,845	Applicant(s) SHOJI, SHOZO	
	Examiner Jeffrey S. Parkin, Ph.D.	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Notice to Comply ...

Detailed Office Action

Status of the Claims

1. Acknowledgement is hereby made of receipt and entry of the preliminary amendment filed 24 September, 2001, wherein claim 4 was amended. Claims 1-8 are pending in the instant application.

Information Disclosure Statement

2. The information disclosure statement filed 31 July, 2001, has been placed in the application file and the information referred to therein has been considered.

3. The reference(s) contained in the information disclosure statement filed 30 October, 2001, have been considered. However, applicants are advised that said reference(s) will not be listed on any patent resulting from this application because they were not provided on a separate list in compliance with 37 C.F.R. § 1.98(a)(1). In order to ensure the printing of said reference(s) on a resulting patent, a separate listing of said reference(s) on a PTO-1449 form must be filed within the set period for reply to this Office action.

35 U.S.C. § 120

4. If applicant desires priority under 35 U.S.C. § 120 based upon a previously filed copending application, **specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph.** The status of non-provisional application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent

application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application. **If applicant desires priority based upon a National Stage filing, this information should also be referenced in the first sentence of the specification (i.e., This application is a National Stage entry of International Application No. PCT/CCPY/NNNNN, filed , 199N).**

37 C.F.R. §§ 1.821-1.825

5. This application clearly fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 (see attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures). Applicants' attention is directed to the final rulemaking notice published at 55 F.R. 18230 (01 May, 1990), and 1114 O.G. 29 (15 May, 1990). If the effective filing date is on or after 01 July, 1998, see the final rulemaking notice published at 63 F.R. 29620 (01 June, 1998) and 1211 O.G. 82 (23 June, 1998). If the effective filing date is on or after 08 September, 2000, see the final rulemaking notice published at 65 F.R. 54604 (08 September, 2000) and 1238 O.G. 145 (19 September, 2000). **Applicant MUST provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy or compact disc copy of the "Sequence Listing", as well as, an amendment directing its entry into the application. Applicant must also provide a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing, and, where applicable, includes no new matter, as required by 37 C.F.R. §§ 1.821(e), 1.821(f), 1.821(g), 1.825(b), and 1.825(d).** If applicant desires the sequence listing in the instant application to be identical with that of another application on file in the Patent and Trademark Office, such request in accordance with 37 C.F.R. § 1.821(e) may be submitted in lieu of a new CRF. Any questions

regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply.

6. Applicant is reminded that sequences appearing in the specification (e.g., see pp. 2-4, 6, 7, 16, and 18) and/or drawings must be identified by a sequence identifier (SEQ ID NO.:) in accordance with 37 C.F.R. § 1.821(d). Sequence identifiers for sequences appearing in the drawings may appear in the Brief Description of the Drawings. Applicant must provide appropriate amendments to the specification and/or drawings inserting the required sequence identifiers. Extensive amendments may necessitate the submission of a substitute specification.

35 U.S.C. § 112, Second Paragraph

7. Claims 1-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Concerning claims 1 and 4-6, claim 1 is vague and indefinite for referencing a "T cell-derived second receptor protein" and a "macrophage-derived second receptor protein" since it is not readily manifest which specific proteins are encompassed by the claim language. T-lymphocytes and macrophages express numerous cell surface receptors and other molecules. However, the reference to a second receptor protein is not understood. Applicant should clearly and unambiguously identify the proteins of interest (i.e., amino acids 169-173 of the second extracellular domain of the CCR5 receptor or amino acids 179-183 of the second extracellular domain of the CXCR4 receptor). Moreover, the claim also fails to clearly set forth the salient chemical structural characteristics of the claimed peptides. For instance, how are the peptides cyclized?

Which amino acid residues are involved. Which portions of the peptide can be modified to accommodate various substituent groups (claims 4 and 5)? Are any of the side groups protected by chemical substituents and unavailable for further modification?

9. Concerning claims 2 and 7, claim 2 is vague and indefinite for failing to clearly set forth the salient structural characteristics of the claimed peptide. The claims reference cyclized peptides but fail to identify those amino acids that are involved in this process. Moreover, it is unclear if the claims reference a parent peptide which comprises a second cyclic peptide linked to the parent sequence. Appropriate clarification and correction are required.

10. The structure set forth in claim 3 is also confusing since it is not readily manifest which amino acid residues were cyclized and which represent normal peptidyl bonds. Applicants should clearly and unambiguously set forth the salient characteristics of the claimed invention (i.e., a linear peptide $H_2N-X_1-X_2-...-X_{11}-X_{12}-COOH$ which has been cyclized at the amino and carboxyl termini through peptidyl bond formation).

35 U.S.C. § 112, First Paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 6-8 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in

the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed toward AIDS vaccines comprising cyclized peptides derived from what appear to be portions of the HIV-1 coreceptors CCR5 and CXCR4.

The legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The claims are of considerable breadth and encompass an inordinate number of cyclized peptides. For instance, claim 1 fails to set forth any of the amino acids present in the peptide of interest. Claim 2 only stipulates that the peptide of interest comprises one or two core five amino acid core sequences. Moreover, the disclosure fails to identify suitable peptides that can reasonably be expected to provide a therapeutic or protective effect against HIV infection.

2) The disclosure fails to identify the molecular determinants of any given peptide that are capable of modulating protective and therapeutic immune responses. One of the problems with HIV vaccine development is that the correlates of protective immunity remain to be elucidated. Thus, it is not readily manifest which immunogens will provide the desired response. The disclosure is silent

concerning this item.

3) The disclosure fails to provide any working embodiments. Considering the unpredictability of the art vis-à-vis HIV vaccine development, the skilled artisan would certainly require a working embodiment before concluding that any given cyclized peptide would prove useful as a therapeutic or protective vaccine.

4) The state-of-the-art pertaining to HIV vaccine development has been characterized by many difficulties and failures (Haynes *et al.*, 1996; Lee, 1997; Letvin, 1998; Burton and Moore, 1998; Moore and Burton, 1999; Johnston, 2000; Bende and Johnston, 2000; Feinberg and Moore, 2002). To date, there is no effective vaccine for the prevention or treatment of HIV-1 or -2 infection. This is due to a number of factors including the *quasispecies* nature of HIV infection which leads to rapid immune escape, a lack of understanding of the correlates of protective immunity thereby precluding the identification of suitable viral immunogens, delivery vehicles, and immunization regimens, the lack of suitable animal models in which to assess vaccine efficacy, the ability of the virus to reside in quiescent T-lymphocytes thereby persisting indefinitely, and a lack of understanding of mucosal immune responses. The disclosure fails to provide any illumination on any of these topics.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Correspondence

13. The Art Unit location of your application in the Patent and Trademark Office has changed. To facilitate the correlation of related papers and documents for this application, all future correspondence should be directed to **art unit 1648.**

14. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette,

1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

15. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, Laurie Scheiner or James Housel, can be reached at (703) 308-1122 or (703) 308-4027, respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

22 June, 2003

09/889,845 Application No.:

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: see P5 of the Office action

Applicant Must Provide:

☒ An initial ~~or substitute~~ computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial ~~or substitute~~ paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE